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Genotype-phenotype relationship study in a large cohort of 1717-1G→A/DeltaF508 CF patients.

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We report here data from the French CF registry on 67 CF patients bearing the 1717-1G→A/DeltaF508 genotype. Each compound heterozygote was matched to a ΔF508 homozygote of same sex, age (± 1 year) and attending the same CF care network.
Both populations were 13 years old at the time of the study, 76% of the patients being younger than 20 years. The mean age at diagnosis was similar in both groups: 18.5 months ± 31.7 versus 20.1 ± 33.2 respectively. No difference was found in the clinical clues at the time of diagnosis, except for a higher frequency of meconium ileus among the 1717-1G→A/ΔF508 patients (24.2% versus 10.9% P=0.04). Both groups had poor nutritional status and a mean BMI under normal values (16.7 versus 16.8 kg/m^2). The mean FEV_1 scores were below 75%. The mean FVC score was lower, but not significantly, in the 1717-1G→A/ΔF508 group than among the ΔF508 homozygotes (77.7 ± 23.4 versus 86.8 ± 22.9 % of predicted value; p = 0.07). However, the median values were closer: 83.3 % versus 85.8%. The mean sweat chloride concentration and the prevalence of clinical events, such as liver cirrhosis and mellitus diabetes, were similar in both groups. Almost all patients were pancreatic insufficient.
In conclusion, the 1717-1G→A allele leads to a severe phenotype indistinguishable from the ΔF508 mutation, but for an increased risk of meconium ileus.
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Detection of Cystic Fibrosis mutations in echogenic bowel

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The presence of echogenic bowel detected on ultrasound investigation during the second trimester of pregnancy can be a normal variant and also associated with cystic fibrosis, as well as a number of other disorders such as chromosome aneuploidy. We have investigated 91 cases of echogenic bowel and have detected cystic fibrosis homozygosity in four of these (4.3%) with the following genotypes: F508del/L732X, F508del/574delA, F508del/F508del, F508del/G542X. In addition heterozygosity was observed in 15 cases (13.4%): 9 with F508del 2 with 621+1G>T and 1 case each for I148T, 2789+5G>A, R297Q and E822X. An additional finding was the presence of particular polymorphisms: 3 instances of 1716G/A (E528E), 2 of 2752-15G/C, 2 of R1162L and 1 of 4029A/G. Our data indicated that the prior risk of CF in a fetus with echogenic bowel for our population is 4.3% and the remaining risk of an heterozygous fetus having CF is between 10.3 and 20%.

Table 1: Summary of families tested and CF results

Both parents and/or fetus negative	21	
One parent carrier- fetus negative	2	I148T, F508del
One parent carrier- fetus not tested	5	621+3A>G, R75Q and 3 with F508del,
One parent carrier- fetus carrier	7	621+1G>T, I148T and 5 with F508del
Both parents carriers- fetus affected	4	F508del/L732X, F508del/574delA, F508del/F508del, F508del/G542X
Fetus only tested- negative	18	
Fetus only tested- carrier	8	E822X; 2789+5G>A; 621+1G>T; R297Q; and 4 F508del
Couple only tested- both negative	26	
TOTAL	91	4 homozygotes and 15 heterozygotes

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CFTR mutations and polymorphisms in patients with disseminated bronchiectasis

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We tested the possible involvement of CFTR mutations and polymorphisms in etiology of disseminated bronchiectasis (DB) of unknown cause, in 19 Serbian patients
The whole coding region and intronic boundaries of the CFTR gene were analyzed by denaturing gradient gel electrophoresis (DGGE) and subsequent DNA sequencing.
In 2/19 patients, two different CFTR mutations were detected. One patient was a compound heterozygote (V920L/R75Q) and one was heterozygous for R75Q. The cumulative allelic frequency of mutations was 7.9% (3/38 alleles). IVS8-5T allele was not found in any of the patients. The incidence of the M470 allele was 28.9% (11/38 alleles). Several common silent mutations (1716G/A, 2694T/G, 4002A/G, 4404C/T) and nucleotide changes in non-coding regions (875+40A/G, GATT6/7, 1011+11C/T) were identified.
Frequency of CFTR mutations obtained in this study was not significantly higher than in general population and our results do not indicate a major role of CFTR gene mutations in the etiology of DB. In spite of the facts that the clinical selection of patients was strict and that the complete coding region of the CFTR gene was screened, due to the small sample size, these results should be considered preliminary and need to be confirmed in a larger study. Recent publications by King et al and Casals et al reported controversial results regarding the involvement of CFTR in development of DB, so further multicentre studies on a larger cohort of clinically well defined patients are needed to resolve these conflicting results.

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Influence of Interleukin-10 on airways colonization by *Aspergillus fumigatus* in cystic fibrosis patients

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Recent evidence suggests that genetic variants affecting the production of interleukin (IL)-10 may play a role in the response to pathogens in cystic fibrosis (CF). The study was designed to seek for an association between alleles carried at position –1082 of the IL-10 promoter and phenotypical data from 378 patients with CF. After adjusting for potential confounding variables a significant relationship was found between the –1082GG genotype and both *A.fumigatus* colonization and allergic bronchopulmonary aspergillosis (ABPA). In addition, higher serum levels of IL-10 were observed in patients chronically infected with *A.fumigatus*, and this was associated with a significant increased frequency of –1082G allele. These genetic and functional studies suggest that promoter variants of IL-10 may predispose to develop *A.fumigatus* colonization and ABPA in CF.